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# EXTENDED SPECTRUM BETA LACTAMASE PRODUCING UROPATHOGENS IN A TERTIARY CARE HOSPITAL IN SOUTH INDIA: A CLINICO MICROBIOLOGICAL STUDY

Microbiology

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## ABSTRACT

**Introduction:** Urinary Tract Infection (UTI) is the most common bacterial infection encountered in both hospital and community setup and the presence of drug resistance carries remarkable clinical implication. Drug resistant phenotypes like ESBL (Extended Spectrum Beta lactamase producers) are difficult to treat causing increased morbidity.

**Aims:** The present study aims to determine the prevalence of ESBL producing Enterobacteriacea among Uropathogens and to determine the Antibiotic susceptibility pattern.

**Materials and Methods :**A total of 726 urine samples were obtained and processed as per standard microbiological techniques .Antibiotic susceptibility testing was done by Kirby Bauer disc diffusion method. All the isolates were screened for ESBL production and confirmed by Double Disc Synergy test (DDST).Differences between the antibiotic susceptibility pattern ,Various risk factors were assessed among the ESBL producing and non ESBL producing bacteria and the significance was analyzed .

**Statistical analysis used:** Chi square test.($p < 0.05$ significant)

**Results:** A total of 726 urine samples were processed of which 421 bacteria belonging to Enterobacteriaceae were included in the study. Most common organism isolated was *Escherichia coli* 279 (66.27%).Highest susceptibility was observed for Imipenem 361 (85.7%) and Amikacin 356 (84.5%).Out of 461 isolates, 235 (55.8%) isolates were positive for ESBL screening all the isolates were confirmed with DDST. There was a significant difference for Diabetes mellitus, CAUTI and Inpatients among the antibiotic susceptibility pattern between ESBL and non ESBL producers.($p<0.0001$)

**Conclusions:** Early detection of Multidrug resistance isolates like ESBL producers in routine testing could help avoid treatment failure. Screening for ESBL production needs to be carried out regularly in every clinical diagnostic laboratory to guide clinicians in proper selection of antibiotics. Continued monitoring of the susceptibility pattern of ESBL producing bacteria will provide valuable information regarding the local antimicrobial susceptibility pattern which in turn will guide in choosing the initial empirical therapy

## KEYWORDS

Antibiotic resistance, ESBL, Urinary tract Infection

## INTRODUCTION:

Urinary Tract Infection (UTI) is the most common bacterial infection encountered in both hospital and community setup.UTI pose a serious health threat with respect to antibiotics resistance .[1]The prevalence of ESBL production ranges from 3.3% to 86.6% among gram-negative bacilli varies widely depending on the geographical location.[2]In a study done in a Tertiary Care Centre in India, ESBL was detected among 68% of gram negative bacteria.[3]The presence of ESBLs among the uropathogens carries remarkable clinical implication as they are difficult to be treated and cause increased morbidity among the patients.[4] ESBL producing uropathogens can transfer the drug resistance to other organisms hence it becomes difficult to treat .Treatment for UTI is usually started empirically .Hence it is essential to study the local Antibiotic susceptibility pattern. The present study aims to determine the prevalence of ESBL producing Enterobacteriacea among Uropathogens and to determine the Antibiotic susceptibility pattern.

## MATERIALS AND METHODS:

The present crosssectional study was carried out at department of Microbiology, for a period of one year (March 2016-February2017). The study was approved by Institutional ethical committee. All Patients with signs and symptoms of urinary tract infections (UTI)in the age group of more than 15 years and both the sexes were included for the study. Urine specimen (clean catch midstream urine and Catheterized urine specimen).Specimens were inoculated in MacConkey agar and blood agar plates and incubated at 37C for 18-24 hrs. All Specimens showing mixed growth of more than three types of colonies were excluded from the study. All specimens with growth of > 100000 CFU /ml were considered as significant and were identified by standard microbiological techniques. Antibiotic susceptibility pattern was performed by Kirby Bauer disc diffusion method with Ampicillin, Amikacin,Cotrimoxazole,Cefotaxime, Ceftazidime, Norfloxacin, Nitrofurantoin and Imipenem and the results were interpreted as per CLSI guidelines. All the isolates showing resistance to Cefotaxime (30g) and Ceftazidime (30g) disks were considered positive for ESBL screening. ESBL screening and were further confirmed by Double Disc Synergy test (DDST) with Cefotaxime (30g), Ceftazidime (30g), and Amoxyclav (10g+20g).[5]

Differences between the antibiotic susceptibility pattern among ESBL and non ESBL producer was analysed by Chi square test and p value < 0.05 was considered as significant. Various risk factors like Renal calculi, Diabetes mellitus, ICU stay for more than 1 week, CAUTI, prior usage of Antibiotics and Inpatients were assessed among the ESBL producing bacteria and non ESBL producing bacteria and the significance was analyzed using p value.(Chi square test)and p value less than < 0.05 was considered as significant.

## RESULTS:

A total of 726 urine samples were processed of which 421 Gram negative bacteria belonging to Enterobacteriacea were isolated. Most common organism isolated was *Escherichia coli* 279 (66.27%), followed by *Klebsiella pneumoniae* 91 (21.61%) (Table 1). overall 235 (61.6%) of the isolates were positive for ESBL screening and all the isolates were confirmed with DDST (table 2).Over all highest susceptibility was observed for Imipenem 361 (85.7%) Amikacin 356 (84.5%), and Nitrofurantoin 352 (83.3%)(Table 3).Escherichia coli showed highest susceptibility for Nitrofurantoin 240(86%) and Imepenem 234(83.8%) .Klebsiella pneumoniae showed highest suceptibililty for Amikacin 86(94.5%).Norfloxacin showed a resistance of 296 (70.3%).ESBL producers were predominantly observed in the intensive care unit (78.8%) followed by surgical ward (65%) and Paediatric ward (54%)(Figure 1).Various risk factors like Renal calculi, Diabetes mellitus, ICU stay for more than 1 week, CAUTI(Catheter associated urinary tract infection), prior usage of

Antibiotics and admission as inpatients were assessed and the significance was analyzed by Chi square test. There was a significant difference for Diabetes mellitus, CAUTI and Inpatients (p<0. 0001). (Table 4)There was a significant difference between the antibiotic susceptibility pattern between ESBL and non ESBL producers. (p<0. 0001).(Table 3)

**Table 1 Distribution of Isolates from urine specimens**

| S.No | Isolate | Number |
|---|---|---|
| 1 | Escherichia coli | 279(66.27%) |
| 2 | Klebsiella pneumoniae | 91(21.61%) |
| 3 | Citrobacter spp | 28(6.65%) |
| 4 | Enterobacter spp | 9(2.13%) |
| 5 | Proteus mirabilis | 8(1.9%) |
| 6 | Proteus vulgaris | 3(0.71%) |
| 7 | Morganella morganii | 3(0.71%) |
| | Total | 421 |

**Table 2 Distribution of Extended spectrum Beta lactamase producing isolates**

| s.no | Isolate | Number (%) |
|---|---|---|
| 1 | Escherichia coli n=279 | 170(60.93%) |
| 2 | Klebsiella pneumonia n= 91 | 59(64.83%) |
| 3 | Proteus mirabilis/Proteus vulgaris n=11 | 6(54.5%) |
| | N=381 | 235(61.6%) |

**Table 3 Evaluation of Antibiotic susceptibility pattern among ESBL Vs Non ESBL producers**

| Antibiotics N=421 | ESBL PRODUCERS sensitive (235) | Non ESBL Producers sensitive (186) | Total susceptibility % |
|---|---|---|---|
| Amikacin | 190 | 166 | 356(84.5%) |
| Ampicillin | 72 | 59 | 131(31.1%) |
| Cefotaxime | 12 | 153 | 165(39.19%) |
| Ceftazidime | 25 | 161 | 186(44.18%) |
| Co-trimoxazole | 66 | 95 | 161(38.24%) |
| Norfloxicin | 33 | 92 | 125(30.40%) |
| Nitrofurantion | 186 | 167 | 353(83.8%) |
| Imepenem | 223 | 138 | 361(85.7%) |

P value : (p<0.0001)

**Table 4 Evaluation of Risk factors among ESBL Vs Non ESBL producers**

| S NO | Risk Factor | | ESBL Producers | Non ESBL Producers | Total | P value |
|---|---|---|---|---|---|---|
| 1 | Renal Calculi | + | 26 | 21 | 97 | 1.000 |
| | | - | 209 | 165 | 379 | |
| 2 | Diabetes Mellitus | + | 124 | 154 | 278 | 0.0001 |
| | | - | 111 | 32 | 143 | |
| 3 | ICU stay > 1 week | + | 15 | 6 | 21 | 0.1775 |
| | | - | 220 | 180 | 388 | |
| 4 | CAUTI | + | 24 | 92 | 116 | 0.0001 |
| | | - | 211 | 94 | 305 | |
| 5 | Prior use of Antibiotics | + | 20 | 12 | 42 | 0.4600 |
| | | - | 205 | 174 | 379 | |
| 6 | In Patients | + | 209 | 154 | 363 | 0.0268 |
| | | - | 26 | 36 | 58 | |

## DISCUSSION:

UTI is one of the commonly encountered bacterial infection affecting 150 million people worldwide every year.[6]The increasing level of antimicrobial resistance among uropathogens is of great challenge since it can limit therapeutic options. ESBL producers are often associated with -resistance to other antibiotics like Aminoglycoside and fluoroquinolones and Cotrimoxazole[7,8].

Escherichia coli was the frequently isolated uropathogen similar to Irenge et al and Krishna kumar et al.[1,4] In the present study we observed highest susceptibility for imipenem, Amikacin and Nitrofurantoin. Norfloxacin showed resistance of 70.5%. This can be attributed to the empirical prescribing practices of Norfloxacin as the first line drug among clinicians before the antibiotic susceptibility report.It was observed that ampicillin was the least susceptible drug in the study

In the present study 235 (61.6%) of the uropathogens were ESBL producers.Various studies have reported ESBL producers ranging from 26% to 75%.[9-13]In our hospital set up though we encountered ESBL producing Uropathogens more in the Medical ICU there was no statistical difference between ESBL and Non ESBL producers in the antibiotic susceptibility pattern(p value : 0.1775).This high prevalence might be attributed to frequent usage of higher antibiotics and faecal carriage of drug resistant strains. It was also observed that there was significant difference in the antibiotic susceptibility pattern among various risk factors like CAUTI ,Diabetes mellitus and admission as Inpatients ESBL and Non ESBL producers. Though ESBL producing organisms are usually associated with patients admitted to a health care set up ,they can also be of community origin [14].

In most cases, the standard disk diffusion tests are effective, and they are still recommended for ESBL detection in routine laboratories [15]. Limitation of our study is that molecular analysis and MIC for ESBL were not carried out. Early detection of these beta– lactamase –producing isolates in a routine laboratory could help avoid treatment failure.Screening for ESBL production needs to be carried out routinely in every clinical diagnostic laboratory to guide clinicians in proper selection of antibiotics. Continued monitoring of the susceptibility pattern of ESBL producing bacteria will provide valuable information regarding the local antimicrobial susceptibility pattern which in turn will guide in choosing the initial empirical therapy.

Conflict of interest : Nil
Acknowledgement: Nil

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